5. (Amended) The polynucleotide according to claim 2, wherein the inducible promoter is a location-specific promoter.

6. (Amended) The polynucleotide according to claim 2, wherein the inducible promoter is a time-specific promoter.

7. (Twice Amended) A polynucleotide complementary to the polynucleotide according to Claim 2.

8. (Twice Amended) A non-human animal into which the gene encoding the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the animal.

9. (Twice Amended) An organ into which the gene encoding the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the organ.

10. (Twice Amended) A tissue into which the gene encoding the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the tissue.

11. (Twice Amended) A cell into which the gene encoding the polynucleotide according to Claim 2 is introduced, wherein an active Cre recombinase is expressed in the cell.

12. (Twice Amended) A method of knocking-in a desired gene in a location controlled and/or time-controlled manner; comprising the steps of:

(1) introducing a first gene construct and a second construct into cells, tissues, organs or whole bodies,

wherein the first gene comprises a polynucleotide according to Claim 2; and the second gene construct comprises a first loxP sequence, a second loxP sequence located

downstream of the first loxP sequence, a second promoter sequence located upstream of the first loxP sequence, and the desired gene located downstream of the second loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled and/or time-controlled manner, and

(3) placing the desired gene under control of the promoter sequence in the second gene construct by site specific recombination on the second gene construct by Cre recombinase expressed in step (2), thereby knocking-in the desired gene in a location-controlled manner and/or time-controlled manner.

13. (Twice Amended) A method of knocking-out a desired gene in a location controlled and/or time- specific manner, comprising the steps of:

(1) introducing a first gene construct and a second gene construct into cells tissues organs or whole bodies,

wherein the first gene construct comprises a polynucleotide according to Claim 2; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a promoter sequence located upstream or downstream of the first loxP sequence, and the desired gene located downstream of the promoter and the first loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled manner, and

(3) inserting a part or whole of the desired gene from the second gene construct by site specific recombination with the second gene construct mediated by Cre recombinase expressed in step (2), thereby knocking-out at least a part or whole of the desired gene, in a location-controlled and/or time-controlled manner.

14. (Amended) The method of claim 12, wherein the desired gene is selected from the group consisting of a xenograft antigen, carcinogenic antigen, and anti antibody-production-associated-molecule antibody.

18. (Amended) An organ from the transgenic animal according to claim 16.

19. (Amended) A tissue from the transgenic animal according to claim 16.

20. (Amended) A cell from the transgenic animal according to claim 16.

21. (Amended) A method for treating a disease caused by malfunction of an organ, comprising a step of transplanting the organ according to Claim 18, into an organism.

23. (Amended) A method for treating a disease caused by malfunction of a tissue, comprising a step of transplanting the tissue according to Claim 19 into an organism.

24. (Amended) A method for treating a disease caused by malfunction of a cell, comprising a step of transplanting the cell according to Claim 20 into an organism.

Please add the following claims:

25. (New) The polynucleotide of claim 2, wherein the modified Cre recombinase gene comprises SEQ ID NO:1.

26. (New) The polynucleotide of claim 25, further comprising at least one of a marker gene, a nucleic acid encoding a nuclear transport signal, and a Kozak sequence.

27. (New) The polynucleotide of claim 25, wherein the inducible promoter is a location-specific promoter.

28. (New) The polynucleotide according to claim 25, wherein the inducible promoter is a time-specific promoter.

29. (New) A polynucleotide complementary to the polynucleotide according to Claim 25.

30. (New) A non-human animal into which the gene encoding the polynucleotide according to Claim 25 is introduced, wherein an active Cre recombinase is expressed in the animal.

31. (New) An organ into which the gene encoding the polynucleotide according to Claim 25 is introduced, wherein an active Cre recombinase is expressed in the organ.

32. (New) A tissue into which the gene encoding the polynucleotide according to Claim 25 is introduced, wherein an active Cre recombinase is expressed in the tissue.

33. (New) A cell into which the gene encoding the polynucleotide according to Claim 25 is introduced, wherein an active Cre recombinase is expressed in the cell.

34. (New) A method of knocking-in a desired gene in a location controlled and/or time-controlled manner; comprising the steps of:

(1) introducing a first gene construct and a second construct into cells, tissues, organs or whole bodies,

wherein the first gene comprises a polynucleotide according to Claim 25; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a second promoter sequence located upstream of the first loxP sequence, and the desired gene located downstream of the second loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled and/or time-controlled manner, and

(3) placing the desired gene under control of the promoter sequence in the second gene construct by site specific recombination on the second gene construct by Cre recombinase expressed in step (2), thereby knocking-in the desired gene in a location-controlled manner and/or time-controlled manner.

35. (New) A method of knocking-out a desired gene in a location controlled and/or time- specific manner; comprising the steps of:

(1) introducing a first gene construct and a second gene construct into cells tissues organs or whole bodies,

wherein the first gene construct comprises a polynucleotide according to Claim 25; and the second gene construct comprises a first loxP sequence, a second loxP sequence located downstream of the first loxP sequence, a promoter sequence located upstream or downstream of the first loxP sequence, and the desired gene located downstream of the promoter and the first loxP sequence,

(2) expressing a Cre recombinase gene by the inducible promoter in a location-controlled manner, and

(3) inserting a part or whole of the desired gene from the second gene construct by site specific recombination with the second gene construct mediated by Cre recombinase expressed in step (2), thereby knocking-out at least a part or whole of the desired gene, in a location-controlled and/or time-controlled manner.

SUPPORT FOR THE AMENDMENTS

Support for Claims 25-35 is found on page 4, lines 17-19 and Claims 1-24. Support for the amendment to Claim 2 is found in Claim 1. Support for the amendment to Claims 8-11 is found, for example, on page 4, lines 11-15. No new matter is believed to have been added by these amendments.